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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/874,390	06/04/2001	Henrik Clausen	4305/0J425	5094

7590 04/22/2003

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	13

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,390	CLAUSEN ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-5,8-19,22,25 and 28* is/are allowed.

6)☒ Claim(s) *20,21,23,24,26,27 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-5 and 8-29 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 1-22-03, paper No.12, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 21 recites the phrase "amplified genomic regions are at least 95% identical to SEQ ID NO:1". It is not clear to the Examiner as to what applicants mean by the above phrase. It is not clear whether applicants mean that the amplified sequence corresponds to the exons only in the cDNA or specific exons in the genomic DNA. This confusion arises because SEQ ID NO:1 does not correspond to the genomic sequence (i.e., both introns and exons) of C2/4GnT.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening for DNA sequence variations in the cDNA such as the polynucleotide with SEQ ID NO:1, encoding the human C2/C4GnT polypeptide by amplifying the cDNA by PCR and detecting the variation by DNA sequencing or SSCP does not reasonably provide enablement for such a method to screen variations in a) a genomic DNA encoding the above polypeptide, b)screen sequence variations in an exon and further the specification does not reasonably provide enablement for screening and detecting mismatch mutations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 21 and 24 are so broad as to encompass methods which have not been taught in the specification. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the different methods broadly encompassed by the claims. Applicants claim a method of screening nucleotide changes n genomic DNA encoding the above polypeptide. However, the specification does not provide the entire genomic sequence of the above gene complete with the sequences of introns and exons. Similarly, claims are drawn to

detect nucleotide changes in an exon. However, the specification does not teach the specific exons and their specific sequences for those skilled in the art. The specification provides the information of only a single exon as in figure 8 and provides the sequences of two primers which can be used. However, the specification is silent regarding the existence of any other exons and their structure. The specification provides the sequence of the cDNA. However, the cDNA information is totally useless for those intending on screening changes in exons or genomic DNA. Similarly, the specification is silent regarding the mismatch mutations. Identification of mismatch mutations without prior knowledge as to which regions of the nucleotide sequence has such mutations is not only unpredictable but also improperly extensive and imposes undue burden on those skilled in the art. Therefore, in order to for the claims to be fully enabled, there is a requirement of knowledge of and guidance with regard to the genomic polynucleotide sequence, the identification of specific exons in the above genomic DNA and identification of mismatch mutations. However, in this case the disclosure is limited to the cDNA sequence only.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for genomic clones or exons with just a cDNA clone. Methods of identifying exons using the cDNA information with a reasonable expectation of success is unpredictable.

The specification therefore does not support the broad scope of the claims which encompass methods of screening genomic DNA, exons and mismatch mutations because the specification does not establish: (A)the specification does not provide a fully annotated genomic sequence information for the above enzyme; (B) the specification does not teach as to how many exons exist in the above gene and the specific sequence of each of the exons; (C) a rational and

predictable scheme for identifying mismatch mutations in the above gene; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of screening genomic sequences of the above gene and method of identification of mismatch mutations. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, performing the above methods and obtaining the desired results is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection arguing that the claim amendments overcomes the above rejection. However, such amendments are not persuasive to overcome the rejection of claim 21 or the new claim 24.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making the polynucleotide with SEQ ID NO:2 having C2/4GnT activity, does not reasonably provide enablement for making function conservative variants of the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claim 20 is so broad as to encompass methods which have not been taught in the specification. The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the method of making all function conservative variants broadly encompassed by the claims. Applicants claim a method of making function conservative variants whrein the amino acid sequence is modified using other amin oacids at one or more positions. However, the specification does not teach as to which specific amino acid can be modified with which amino acid from among the 20 naturally occurring amin acids such that the modified polypeptide continues to be functional. Therefore, in order to for the claims to be fully enabled, there is a requirement of knowledge of and guidance with regard to the regions of the polypeptide that can be modified and specific residues that can be modified either by deleting, inserting or substituting with other specific amino acids. However, in this case the disclosure is limited to the method of making only one polypeptide with SEQ ID NO:2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any

protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any galactosyltransferase because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the specific activity; (B) the general tolerance of the above polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in the polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all function conservative variants with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, method of making the polypeptide having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 20 is directed to a method of making a genus of DNA molecules comprising function conservative variants of SEQ ID NO:2. The specification does not contain any disclosure of the structure of all the function conservative variant sequences that comprise the genus of claim 20. The genus of polypeptides that comprise these above molecules is a large variable genus with the potentiality of having many different structures. Therefore, many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses the method of making only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Newly added claims 23, 26-27, 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules comprising fragments of SEQ ID NO:1 (i.e., nucleotides 634-1812). The specification does not contain any disclosure of the function of all DNA sequences that comprise fragments of SEQ ID NO:1. The genus of DNAs that comprise these above DNA

molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Allowable Subject Matter

Claims 1-5, 8-19, 22, 25, and 28 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
April 18, 2003